UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: Updated Review of Poison Control Center Data for Residential Exposures to Rodenticides, 1993-1996

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I. INTRODUCTION

Most of the nation's Poison Control Centers (PCCs) participate in a national data collection system, now known as the Toxic Exposure Surveillance System (TESS). Some 64-67 Centers at hospitals or universities participated from 1993 through 1996 (Litovitz et al. 1994-1997). PCCs provide telephone consultation for individuals and health care providers, 24 hours a day/365 days a year. An average of 81% of the U.S. population was covered by PCCs participation in data collection from 1993 through 1996.

The current review is based on 424,644 records of pesticide-related exposures (excluding cases exposed to multiple products, attempted suicides, malicious intent, and confirmed non-exposures) reported to Poison Control Centers participating in TESS from 1993 through 1996. Of the 424,644 exposures, 388,621 occurred in a residential setting and 48,691 of these were due to rodenticide exposures in children under six years of age.

II. DETAILED DESCRIPTION OF POISON CONTROL CENTER METHODOLOGY

This section describes Poison Control Centers operation and their nationwide system of data collection. The use of a standardized form for data collection, definition of key data elements, and quality assurance procedures used by the American Association of Poison Control Centers (AAPCC) are outlined.

Poison Centers receive telephone calls from individuals and health care providers seeking information on how to manage an exposure to a poison. Typically the Poison Center itself is run by a hospital or university. "Poison Centers function primarily to provide poison information, telephone management and consultation, collect pertinent data, and deliver professional and public information" (AAPCC 1988). Each center must have a poison information specialist available on site at all times. Written operational guidelines must be used to assure a consistent approach to the handling of all poison exposures. Included in the guidelines must be a provision for follow-up of each case to determine patient's final disposition or medical outcome.

Participating Poison Control Centers must have a board certified physician on call with medical toxicological expertise. The calls are initially handled by a poison information specialist who has been trained and certified by examination. Approximately 13% of their calls come from doctors treating exposed patients. The other 87% come from victims of the exposure or their relatives (e.g., mother of an exposed child). Regular case reviews and audits are scheduled to assure quality assurance of the data collected. Records kept on all cases must have sufficient narrative to permit review.

The Poison Centers participating in the Toxic Exposure Surveillance System (formerly the National Data Collection System) complete a form or computer record describing each case that contains standard data elements and a narrative section. Information collected includes the date of call, age and sex of the victim, location of victim at time of exposure (e.g., home, work place), substance exposed to, route of exposure, initial symptom assessment, treatment received (e.g., referred to physician, hospitalized), and an evaluation of medical outcome after case follow up. Starting in 1993 information about specific symptoms

reported was also collected. Data are then sent to the AAPCC for processing (AAPCC 1988).

Patients treated at home or any other non-health care site are classified as "managed on site" (Interpretation of the AAPCC Data, AAPCC 1994). Those seen in a health care facility may be classified as either treated and released or admitted for medical care. "Admitted for medical care" is used when "the patient is observed and/or treated and subsequently admitted as an inpatient primarily to receive medical care rather than psychiatric evaluation".

When symptoms or signs occur and follow up is complete, they are categorized into minor, moderate, or major depending on their severity and whether recovery is complete. Definitions used by the Poison Control Centers to categorize medical outcome are given in summary form below (Veltri et al. 1987).

Minor: Minimal symptoms or signs with no residual disability (e.g., mild gastrointestinal symptoms, skin irritation, drowsiness).

Moderate: Symptoms or signs are more pronounced, prolonged, or more of a systemic nature than minor symptoms with no residual disability. Usually some form of treatment is indicated. Examples include: high fever, disorientation, hypotension which rapidly responds to treatment and isolated brief seizures.

Major: Symptoms or signs are life-threatening or result in residual disability or disfigurement. Examples include patients who require intubation plus mechanical ventilation, who sustain repeated seizures, cardiovascular instability, or coma.

Data quality issues

Validity of the data collected by different poison centers is an important concern of the Toxic Exposure Surveillance System. Some 60-70 Centers staffed by six or more personnel each are responsible for collection of the information on each case, properly coding the information and submitting it to the AAPCC

which maintains the national database. Reporting by individual PCCs is dependent on how well their service is known and advertised.

Poison Centers collect data on each call they receive and transfer the information to the Toxic Exposure Surveillance System. The AAPCC conducted an audit of 588 randomly-selected pesticide charts based on records submitted to the TESS in 1996 (AAPCC 1998). Thirty-four cases were excluded from a Center that was over-represented in the data set and another 24 cases were excluded because of three Centers that had closed since 1996. After these exclusions, requests for 530 cases were sent to the PCCs and 512 records were located and returned to the AAPCC for a response rate of 96.6%. Thirteen records could not be located, one Center did not send the three requested records, and the wrong record was sent in two cases. Cases were reviewed to determine how accurately the information coded in TESS matched the information in the original medical record. Five fields important to this analysis were selected for the audit: reason for exposure, route of exposure, management site of case, medical outcome, and accuracy of specific and generic substance category.

Results from the audit found the majority of cases were coded correctly (AAPCC 1998). Of those cases that did contain errors, the most common error was insufficient follow-up to accurately code the flow of patient care or medical outcome. Reason for exposure was coded correctly 90.4% of the time, incorrectly coded in 4.5%, and insufficient information to determine coding in 5.1%. Route of exposure was coded correctly in 95.9% of cases and incorrectly coded in 3.7% (1.7% incorrect route and 2.0% route(s) omitted). Health care facility use and referral was correctly coded for 93.5%, incorrect in 1.8%, and unable to determine correct coding in 4.7%. Outcome was correctly coded in 82.8%, coded incorrectly in 5.1%, and unable to determine correct coding in 12.1% (due to inadequate follow-up or missing information). Substance was correctly coded 93.3% of the time, incorrectly coded 6.5%, and unable to determine if correct 0.2%. Generic code was coded correctly 98.1% of the time and incorrectly coded 1.7% of the time.

Many poisoning cases seen in emergency rooms or by private physicians do not result in calls to a PCC. A study of all acute care hospitals in Utah compared all inpatient and outpatient records of poisoning with calls to the Poison Center serving Utah

and found that only about one-third of the cases matched (Veltri et al. 1987). Characteristics of unmatched cases were not studied so it is not possible to say how PCC cases might differ from hospital cases that do not result in a call to a PCC.

Each Poison Center must keep records on all cases handled by the Center in a form that is acceptable as a medical record (AAPCC 1988). The standardized form or computer record that is used must contain all data elements filled out and sufficient narrative to permit peer review and medical or legal audit. The data must be submitted to the AAPCC's Toxic Exposure Surveillance System within deadlines and meet quality requirements as specified in guidance of the AAPCC.

Most of the cases (83%) submitted to the Toxic Exposure Surveillance System come from certified Poison Control Centers. To be certified a PCC must fulfill the following criteria (AAPCC 1988):

1. Have a board certified physician on-call at all times with expertise in medical toxicology.
2. Have poison specialists available to handle all calls. These specialists are required to complete a training program and are certified by the AAPCC.
3. Maintain a comprehensive file of toxicology information sources and have ready access to a major medical library.
4. Maintain operational guidelines which provide a consistent approach to evaluation and management of toxic exposures.
5. Have an ongoing quality assurance program including regularly scheduled conferences, case reviews and audits.
6. Keep records on all cases handled by the Center with data elements and sufficient narrative to allow for peer review.
7. Submit all case data to the Toxic Exposure Surveillance System, meet deadlines and quality requirements and include all required data elements. Taken together all these criteria help assure the quality of the data.

Examination of AAPCC annual reports from 1993 through 1996 found that 7 states had little or no coverage during that period (Litovitz et al. 1994-1997). They were Arkansas, Illinois, Maine, Mississippi, Oklahoma, South Carolina, and Vermont. Another 5 states (Iowa, Minnesota, Nevada, North Carolina, and Texas) had little or no coverage for one or two of the four years. Of the 81 organophosphate-related deaths reported from 1979 through 1992, 34%

occurred in these 12 states that did not consistently report to the TESS (CDC 1997). Thus, cases of poisoning are under-represented in AAPCC data. Estimated proportion of the U.S. population served from 1993 to 1996 ranged from 70% to 87%, with an average of 81%.

Over-reporting may also occur when symptoms are reported over the phone which cannot be confirmed by a physician or laboratory tests for exposure or effects. Though about 13% of cases are referred to the PCC by a physician, the majority involve a phone call from the victim or relative. Poison Specialists must rely on their experience and judgment to determine which cases have symptoms consistent with the toxicology, dose, and timing of the exposure. While some misclassification can be expected to occur from this approach, it is not expected to be differentially biased among pesticides. That is, there is no reason to believe that Poison Specialists are likely to misclassify one organophosphate more or less than another.

Steps followed to prepare electronic files for analysis

1. Four files, one for each year 1993-1996, were provided by AAPCC in a dBASE 3+ format. Files covered all case records related to insecticides, herbicides, rodenticides, fungicides, moth repellents, and disinfectants.

2. The four files were appended to each other to create one single file containing a total of 459,748 records.

3. Records coded as confirmed non-exposure (outcome=9) were deleted from the file.

4. Records coded as suspected suicidal (reason=9), intentional abuse (reason=11), unknown, but intentional (reason=12), malicious (reason=14), or unknown reason (reason=18) were deleted from the file.

5. Records involving exposure to two or more products (generic_2>1 or Subst_no>2) were deleted from the file.

6. After making the above deletions, there were 424,644 records of unintentional exposures to single products. This file was the basis for all further analyses.

7. Summary fields were created to capture three age classes: adult (20 years or older), children 6-19 years old, and children under age six. Then the "Replace" command was used to substitute the appropriate name for the age class (e.g., Replace Ageclass with 'Child' for age < 6 .and. Age_unit = 1). Summary fields were also prepared to identify cases seen in a health care facility (HCF), treated and released, hospitalized, and seen in a critical care unit. Then the "Replace" command was used to substitute a '1' in the field meeting the appropriate criteria (e.g., Replace HCF with 1 for Ref_tohcf >= 1 .and. Ref_tohcf < 4). The dBASE 3+ file was imported into Microsoft Access 2.0 for further analysis. See detailed instructions covering steps 1-7 in Appendix 1.

8. A table of 8,874 product brand names and their associated generic codes were generated using Microsoft Access Query command which list all records with a unique product name (Sub1txt) and generic code (generic_1). Two fields were added to this file, a field called "ACTIVE", to identify the active ingredients in each product and a field called "TYPE" to identify the category that each generic code fell into (e.g., organophosphate insecticide, anticoagulant rodenticide). The ACTIVE code was completed by using the EPA REFS files or Silver Platter Pestbank to identify the six digit PC code for the primary active ingredient. The TYPE field was completed by using the Microsoft Access update query function. This permits assigning the term 'Anticoag' to the TYPE field for all product brand names assigned generic codes 48563 (short-term acting anticoagulants) and 48564 (long-term acting anticoagulants).

9. The new table of product brand names with associated active ingredient codes and pesticide types was linked to the primary data set of 424,644 exposures using a one-to-many relationship on the primary key field, product brand name (Sub1txt) and enforcing referential integrity. This permits subsetting and cross-tabulating the data by product brand name, generic code, active ingredient, or pesticide type.

III. RESULTS

Results are presented below in tabular form for seventeen types of pesticides. Table 1 presents the number of cases reported by pesticide type and age class. Table 2 presents the number of exposures, symptomatic cases, and type of health care for children.

Table 1. Number of unintentional residential exposures by pesticide type and age class reported to Poison Control Centers, 1993-1996.

Pesticide type	Child<6	Children 6-19	Adults	Total
Anticoagulant	48691	1546	1668	51905
Boric acid	10012	647	1249	11908
Carbamate	11012	2028	9298	22338
Fumigant	154	110	750	1014
Fungicide	1399	365	1899	3663
Herbicide	7621	2269	13776	23666
Hypochlorite disinfectant	9860	1776	5691	17327
Moth repellent	16234	1064	2514	19812
Organochlorine	3957	1551	3478	8986
Organophosphate	24878	5076	32075	62029
Other disinfectant	3476	448	1252	5176
Other insecticide	18934	3153	11583	33670
Other rodenticide	6777	389	1069	8235
Phenol disinfectant	10737	1159	2126	14022
Pine oil	28639	2205	5966	36810
pyrethrins/ pyrethroids	17522	5363	20733	43618
Insect repellents	16547	3539	3324	23410
TOTAL*	237229	32751	118641	388621

* Total includes certain other categories (e.g., molluscicide) not otherwise classified above.

Table 2. Number of unintentional residential exposures, symptomatic cases, cases followed up till medical outcome was determined, cases seen in a health care facility (HCF), and cases hospitalized reported to PCCs for children under six years of age, 1993-1996.

Pesticide type	Exposures	Symptomatic/ Outcome determined	HCF	Hospital.
Anticoagulant	48691	683/22017	16689	341
Boric acid	10012	259/3818	762	28
Carbamate	11012	986/4891	1042	69
Fumigant	154	15/77	35	4
Fungicide	1399	111/584	95	5
Herbicide	7621	987/4152	634	45
Hypochlorite disinfectant	9860	2464/6224	982	34
Moth repellent	16234	651/9033	3054	180
Organochlorine	3957	746/2711	1552	249
Organophosphate	24878	2792/12157	3163	482
Other disinfectant	3476	847/2040	429	15
Other insecticide	18934	1725/8583	1880	253
Other rodenticide	6777	181/2952	2526	105
Phenol disinfectant	10737	2427/5774	669	27
Pine oil	28639	5220/17253	3880	236
pyrethrins/ pyrethroids	17522	2949/8938	2265	100
Insect repellents	16547	3594/8776	1222	44
TOTAL*	237229	26667/120418	41009	2230

* Total includes certain other categories (e.g., molluscicide) not otherwise classified above.

Figures 1-4 present the same information in Table 2 but in graphical form. Figure 5 presents the percent of cases with outcome determined that were symptomatic. These bar graphs show that anticoagulant rodenticides are the leading cause of exposures in children under the age of six years, but a relatively minor cause of symptomatic cases and the lowest percent of cases classified as symptomatic (defined as having minor, moderate, or major medical outcome). Anticoagulant rodenticides are, by far, the leading cause of visits to health care facilities in children under the age of six years and the second leading cause of hospitalization after organophosphate insecticides.

Residential exposures account for 97.4% of all the rodenticide exposures among children under six years of age. Another 1.3% are classifed as occurring in a public area and the remainder in miscellaneous sites, including other and unknown. Of the cases occurring in a residence, 92% occur in the child's own residence and 8% occur in another residence (e.g., grandparents').

When individual age is examined, children aged one or two years account for 69% of all the exposures occurring to children under age six. Table 3 presents the number, percent, and cumulative percent for children by age.

Table 3. Number of children under age six exposed to anticoagulant rodenticides in a residential setting, reported to Poison Control Centers, 1993-1996.

Age in years	Number exposed	Percent	Cumulative percent
0	7,019	14%	14%
1	18,152	37%	52%
2	15,532	32%	84%
3	5,404	11%	95%
4	1,785	4%	99%
5	667	1%	100%

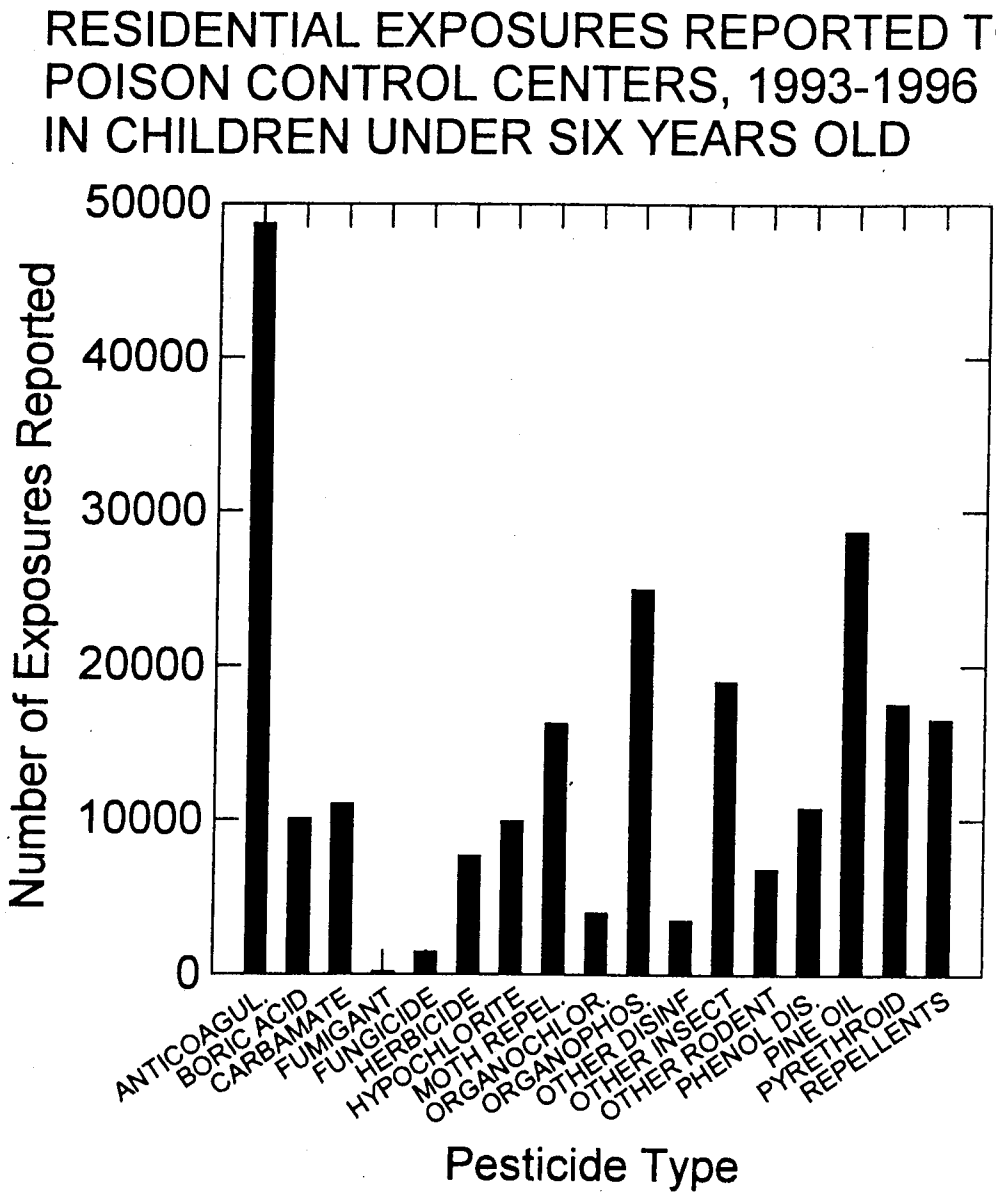

Figure 1. Number of residential exposures reported to Poison Control Centers, 1993-1996, in children under six years old by pesticide type.

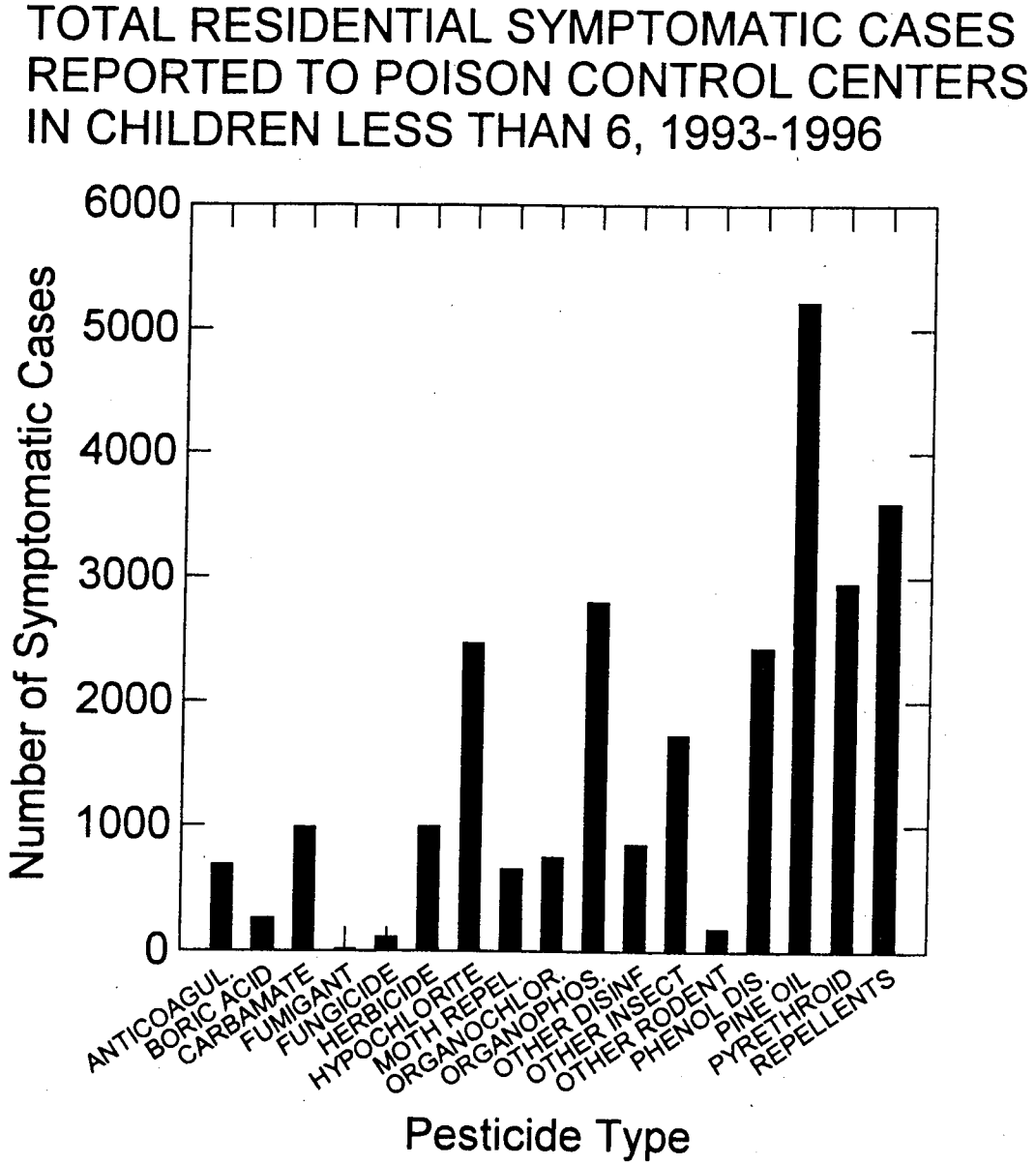

Figure 2. Number of symptomatic residential cases (where outcome was known) reported to Poison Control Centers, 1993-1996, in children under six years old by pesticide type.

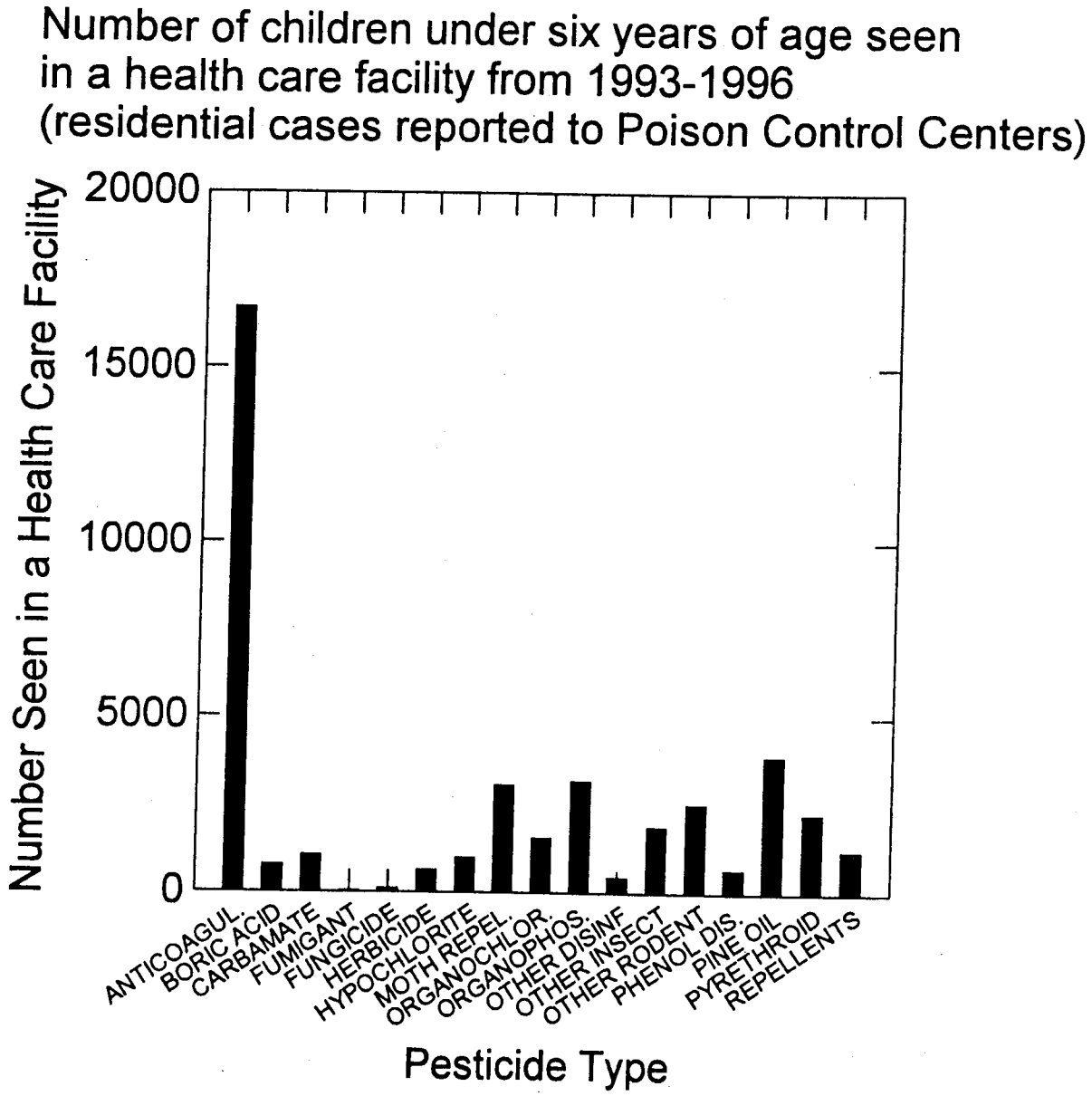

Figure 3. Number of cases seen in a health care facility reported to Poison Control Centers, 1993-1996, in children under six years old by pesticide type.

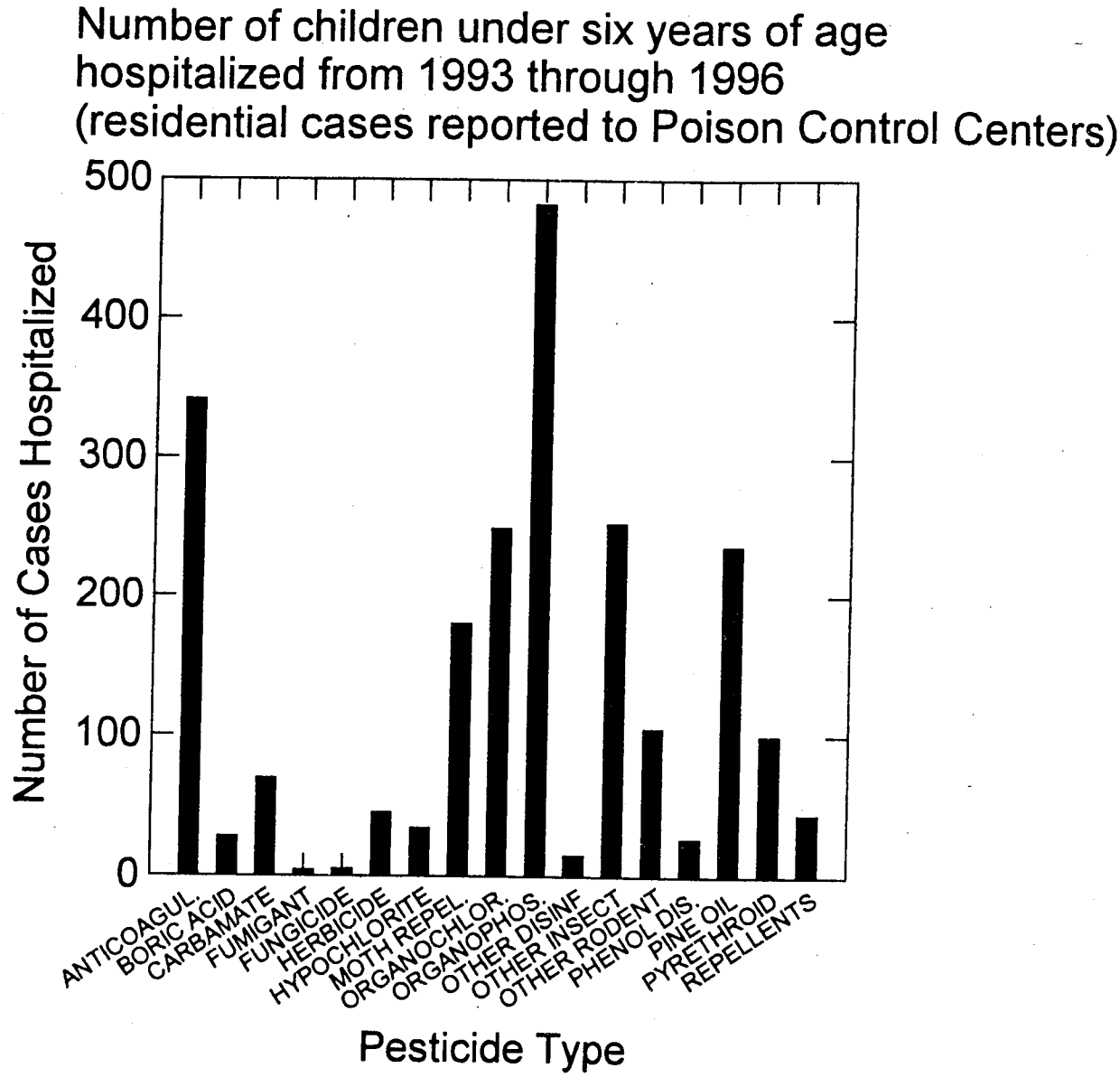

Figure 4. Number of hospitalized cases reported to Poison Control Centers, 1993-1996 in children under six years old by pesticide type.

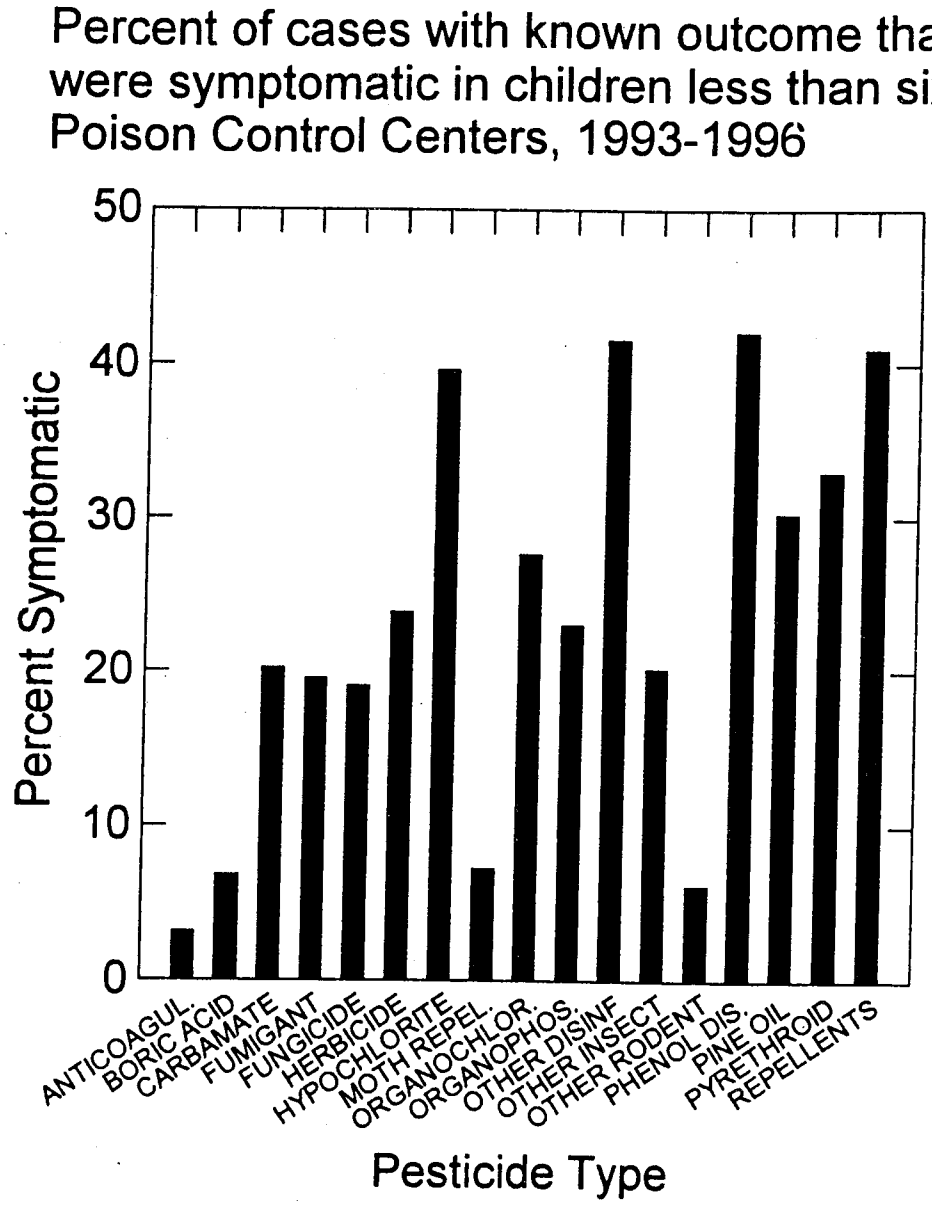

Figure 5. Percent of cases with known outcome that were symptomatic in children under six years old, reported to Poison Control Centers, 1993-1996, by pesticide type.

A primary measure of hazard is the incident rate defined as the number of individuals who become ill divided by the number at risk over some time period. A surrogate measure for the population at risk was developed by estimating the extent of pesticide use in residential households. The EPA survey of home and garden pesticide use provides estimated number of containers and applications of pesticides for all households in the United States in 1990 (Whitmore et al. 1992). Tables 4 and 5 and the corresponding Figures 6 and 7 take the reported exposures and symptomatic cases in young children and estimates the rate of exposure and poisoning (cases defined as minor, moderate, major, or fatal outcome) per million containers in U.S. homes. The purpose of this analysis is to determine whether widespread use rather than some other factor is responsible for a high hazard ranking.

Table 4. Ratio of residential exposures (average per year for 1993-1996) per thousand containers (1990) in U.S. homes for children under six years.

Pesticide type	Exposures per year	Estimated containers (thousands)	Exposures per thousand containers
Disinfectant/ fungicide	54111/4= 13527.75	145,078	0.093
Herbicide	7621/4= 1905.25	32,984	0.058
Insecticide	86315/4= 21578.75	176,454	0.122
Anticoagulant rodenticide	48691/4= 12172.75	4,829	2.521

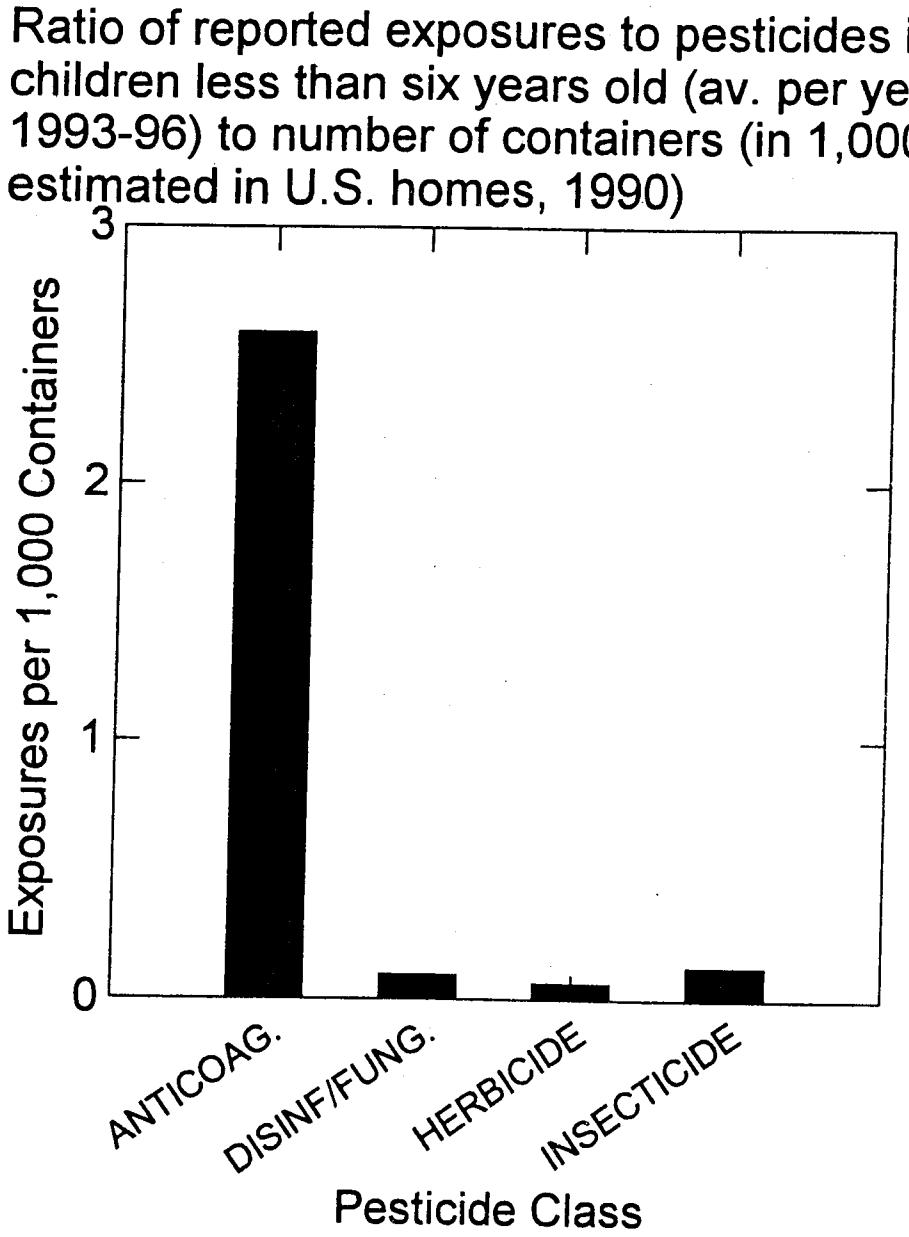

Figure 6. Ratio of reported exposures to pesticides in children less than six years old (1993-1996) to estimated number of pesticide containers in U.S. homes in 1990.

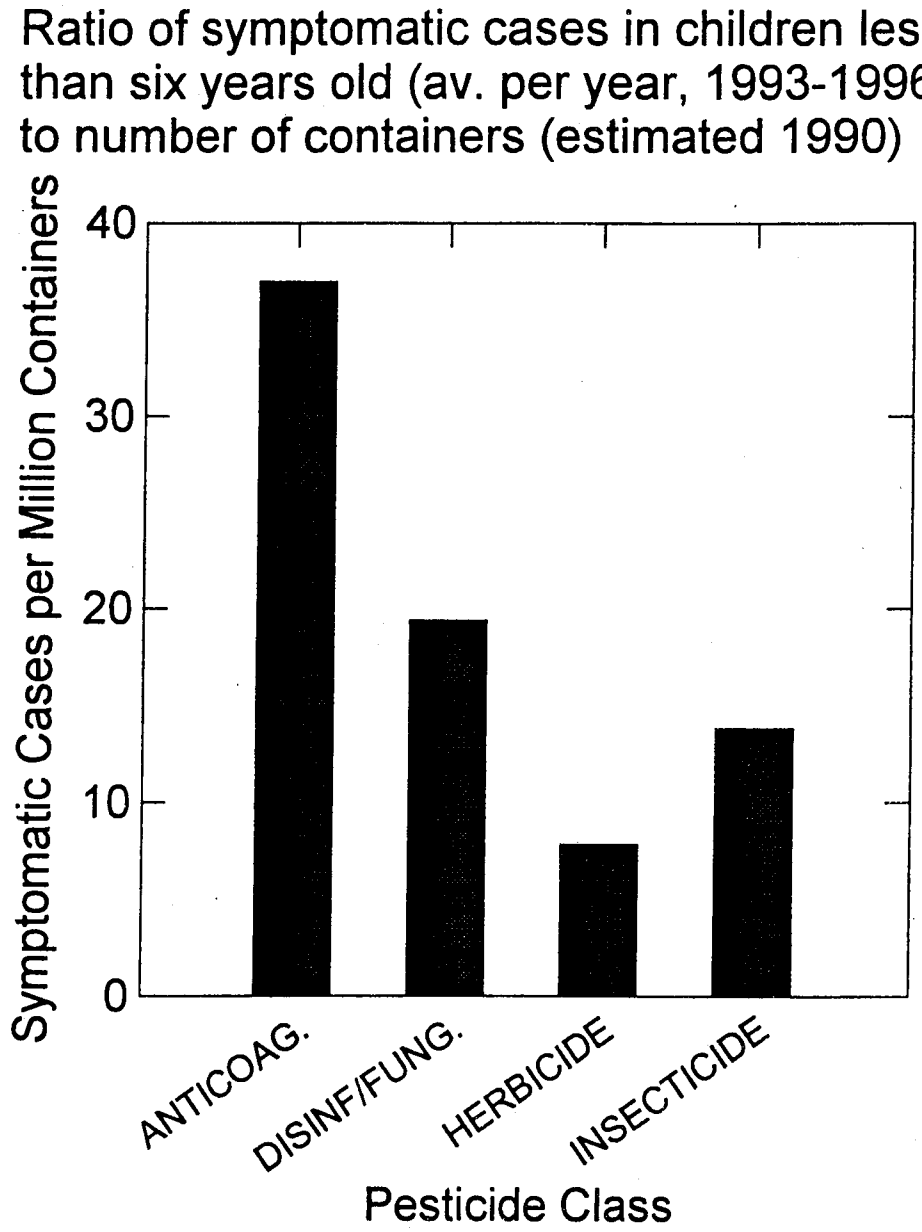

Figure 7. Ratio of symptomatic cases in childreneless than six years old (1993-1996) to estimated number of pesticide containers in U.S. homes in 1990.

Table 5. Ratio of residential symptomatic cases (outcome determined, average per year for 1993-1996) per million containers in U.S. homes in 1990 for children under six years.

Pesticide type	Symptomatic cases per year	Estimated containers (millions)	Symptomatic cases per million containers
Disinfectant/ fungicide	11069/4= 2767.25	145.078	19.07
Herbicide	987/4= 246.75	32.984	7.48
Insecticide	9457/4= 2364.25	176.454	13.40
Anticoagulant rodenticide	683/4= 170.75	4.829	35.36

For children under age six, the ratio is highest for those products typically used or stored close to the floor. The survey of households in 1990 found that about 58% of the disinfectants were stored less than four feet off the floor without a child-resistant closure. For fungicides the figure was 48%, herbicides 19%, insecticides 32%, and rodenticides 46%. Unlike the other types, rodenticides are used almost exclusively as poison baits placed on the floor where children later find them.

Analysis of symptoms and clinical effects of anticoagulant rodenticides by active ingredient

The section examines whether exposure to one type of anticoagulant is more or less likely to result in symptoms than another. Children under six years of age rarely develop clinical effects or symptoms as a result of exposure to anticoagulant rodenticides. Table 6 presents the number of cases with any kind of possibly related symptoms, including such non-specific symptoms as nausea and diarrhea. This table is based on the 683 symptomatic cases reported in Table 2. After adjusting for the number of cases where outcome was determined, the percent cases with symptoms for any one active ingredient is about the same, varying from 3.0-4.5% (see Figure 8).

Table 6. Number of residential symptomatic cases, number where outcome was determined and the percent of symptomatic cases for children under age six exposed to anticoagulant rodenticides, 1993-1996.

Active ingredient	Symptomatic cases	Outcome determined	Percent symptomatic
Warfarin	64	1744	3.7
Brodifacoum	452	15,358	2.9
Bromadiolone	51	1711	3.0
Chlorphacinone	8	222	3.6
Diphacinone	21	772	2.8
Pindone	5	128	3.9
Unknown/ Other	82	2115	3.9

Anticoagulants are known to cause specific symptoms and clinical effects which include reduced clotting, bleeding (e.g., from nose or gums), and bruising. Poison Control Centers capture symptoms related to reduced clotting and bleeding. Table 7 presents the number of cases that develop symptoms specific to anticoagulants including prolonged clotting of blood as measured by prothrombin time and miscellaneous bleeding which can result from exposure to anticoagulants. Also presented in table 7 is the percentage of cases (where outcome was determined) that show these same effects. The information in Table 7 is presented graphically in Figures 9-12.

Table 7. Number and percent of cases (where outcome was determined) reporting prolonged prothrombin time (PT) or other coagulopathy and bleeding (excluding blood in urine or emesis) in children under age six exposed to anticoagulant rodenticides, 1993-1996.

Active ingredient	Prolonged PT/Coagul.	Miscellaneous bleeding	Percent prolonged PT/Coagul.	Percent bleeding
Warfarin	11	3	0.6	0.2
Brodifacoum	95	30	0.6	0.2
Bromadiolone	15	3	0.9	0.2
Chlorphacin.	0	0	0	0
Diphacinone	4	3	0.5	0.4
Pindone	1	0	0.8	0
Unknown/ Other	16	2	0.8	0.1

Brodifacoum was responsible for more cases of coagulopathy and bleeding, but this was because of the far greater number of exposures. When the percent of cases with these factors are compared there is very little difference among the active ingredients. The 0 percents reported for chlorphacinone and pindone must be interpreted with caution since less than 10 symptomatic cases were reported for those two active ingredients.

Zinc phosphide

Though zinc phosphide was not considered in this review, it has had some use as a rodenticide in the home. Among children under six years old, there were 590 exposures from 1993 through 1996, of which 18 were symptomatic and 1 was life-threatening. 361 cases were seen in a health care facility of which 12 were hospitalized. Compared to all pesticides, the percent with symptoms was low but the percent seen in a health care facility was 3.5 times higher than for all pesticides. Zinc phosphide shows a similar pattern to anticoagulant rodenticides, relatively few cases with symptoms but much higher health care provided than for other products.

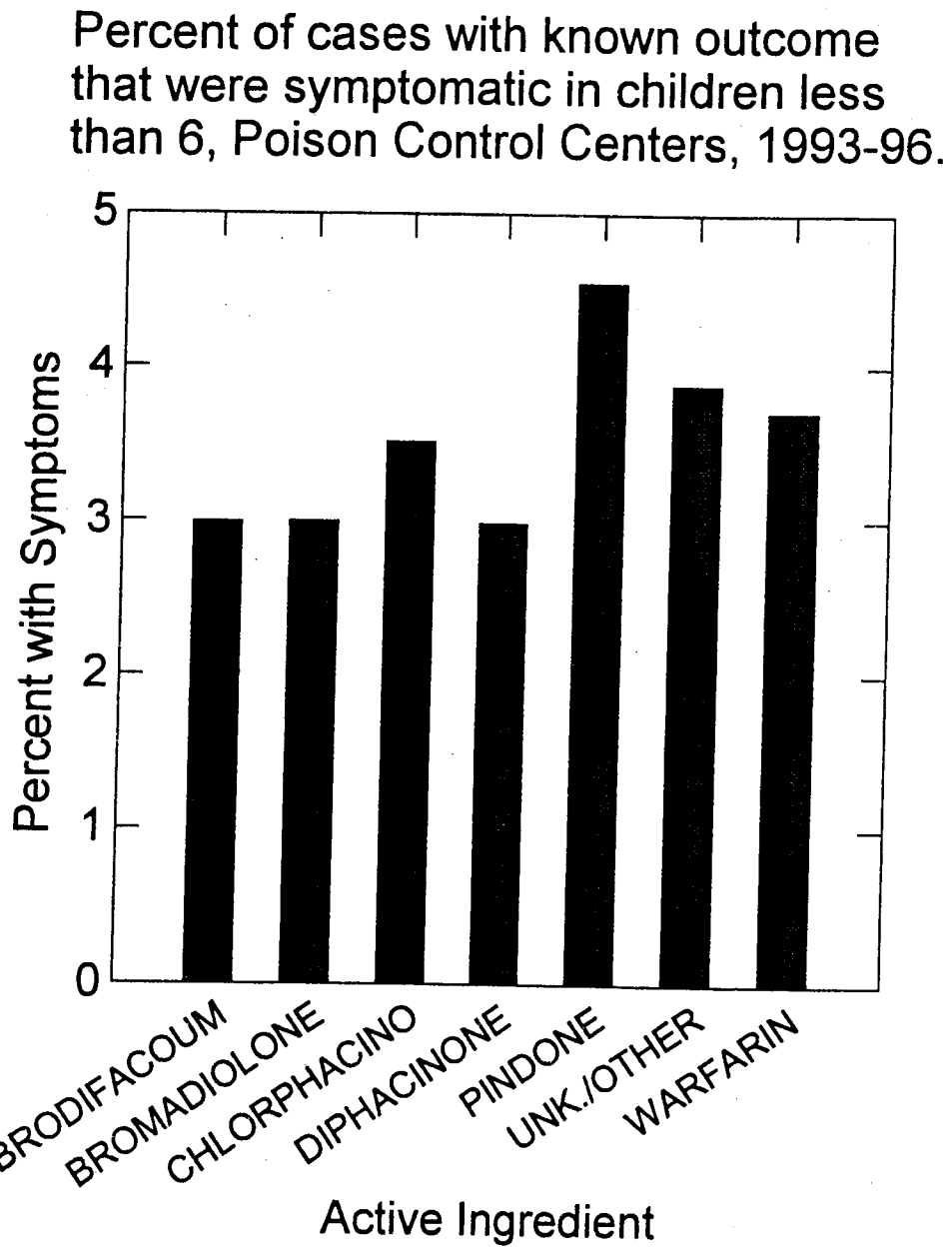

Figure 8. Percent of cases with known outcome with any kind of symptoms among children under six years old reported to Poison Control Centers, 1993-1996, by active ingredient for anticoagulant rodenticides.

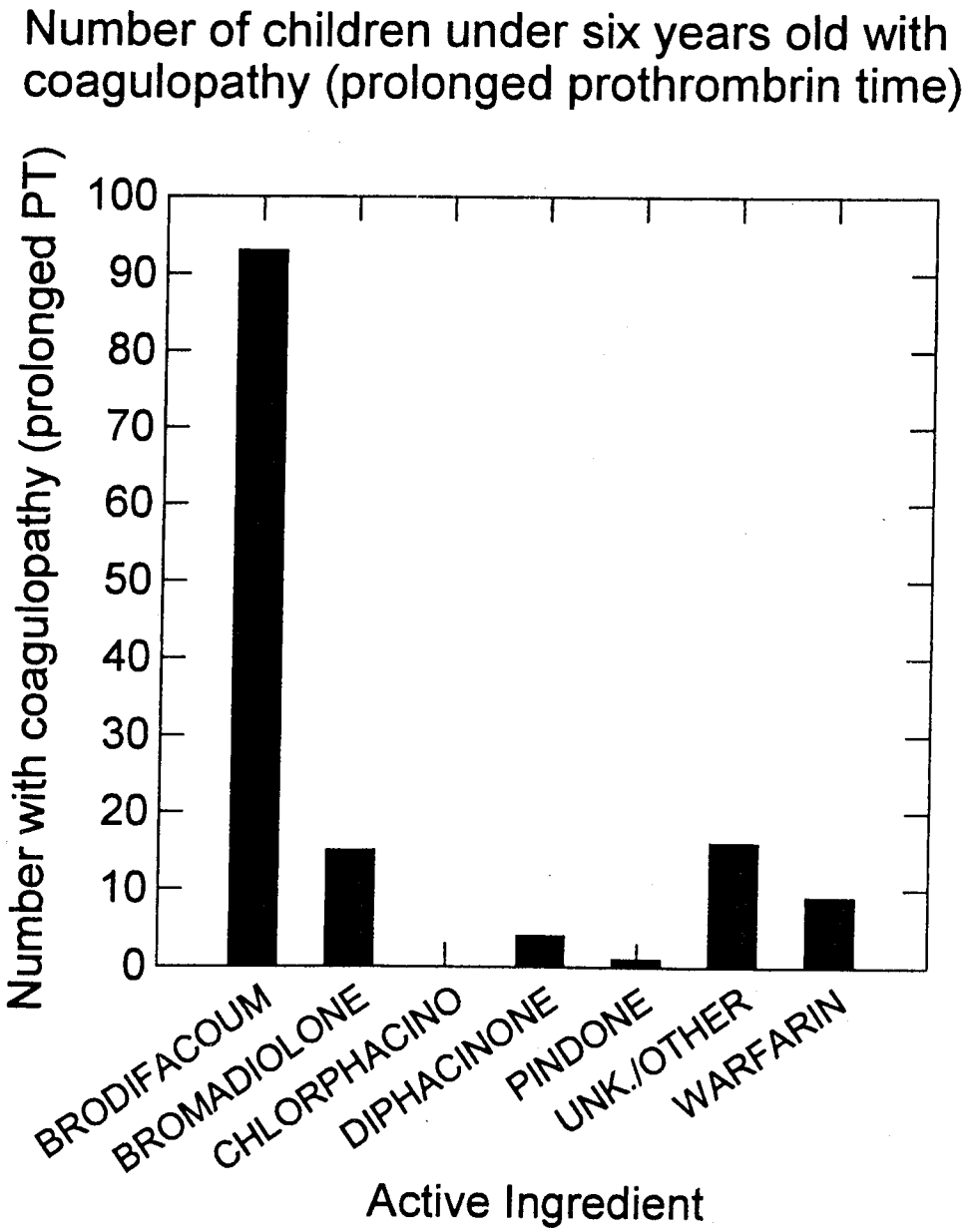

Figure 9. Number of children under six years old with coagulopathy (prolonged prothrombin time) reported to Poison Control Centers, 1993-1996, by active ingredient for anticoagulant rodenticides.

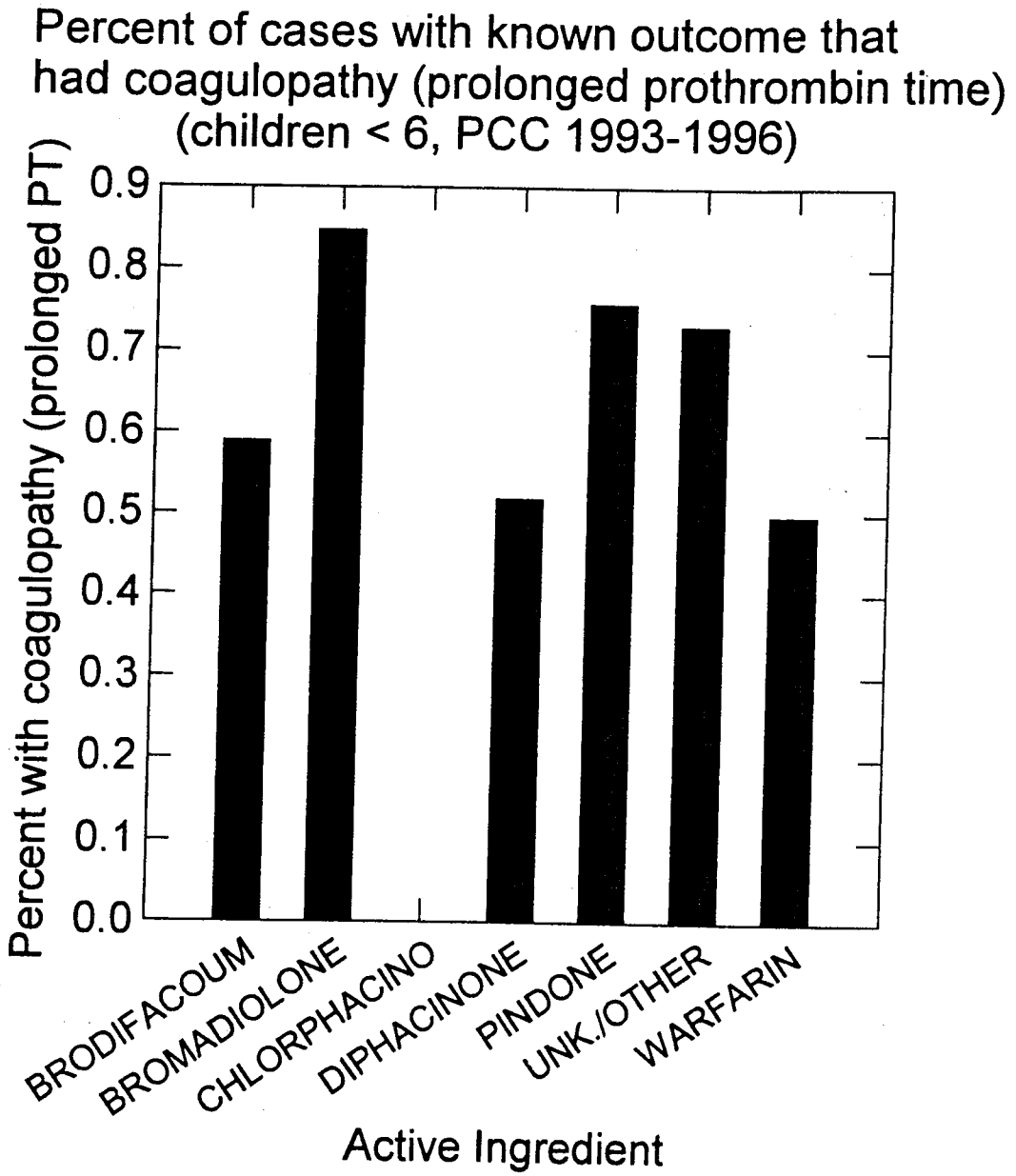

Figure 10. Percent of cases with known outcome that had coagulopathy (prolonged prothrombin time) among children under six years old reported to Poison Control Centers, 1993-1996, by active ingredient for anticoagulant rodenticides.

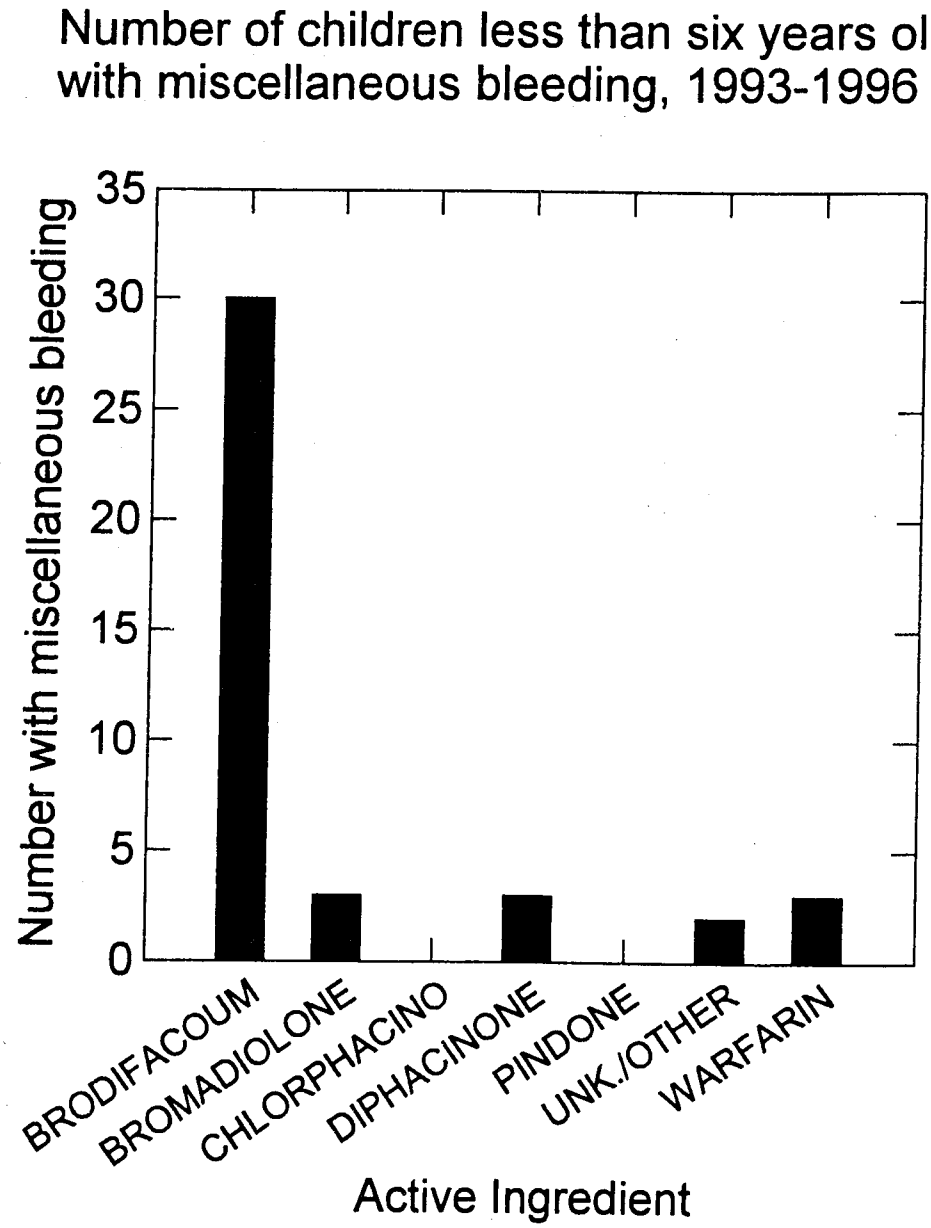

Figure 11. Number of children under six years old with bleeding reported to Poison Control Centers, 1993-1996, by active ingredient for anticoagulant rodenticides.

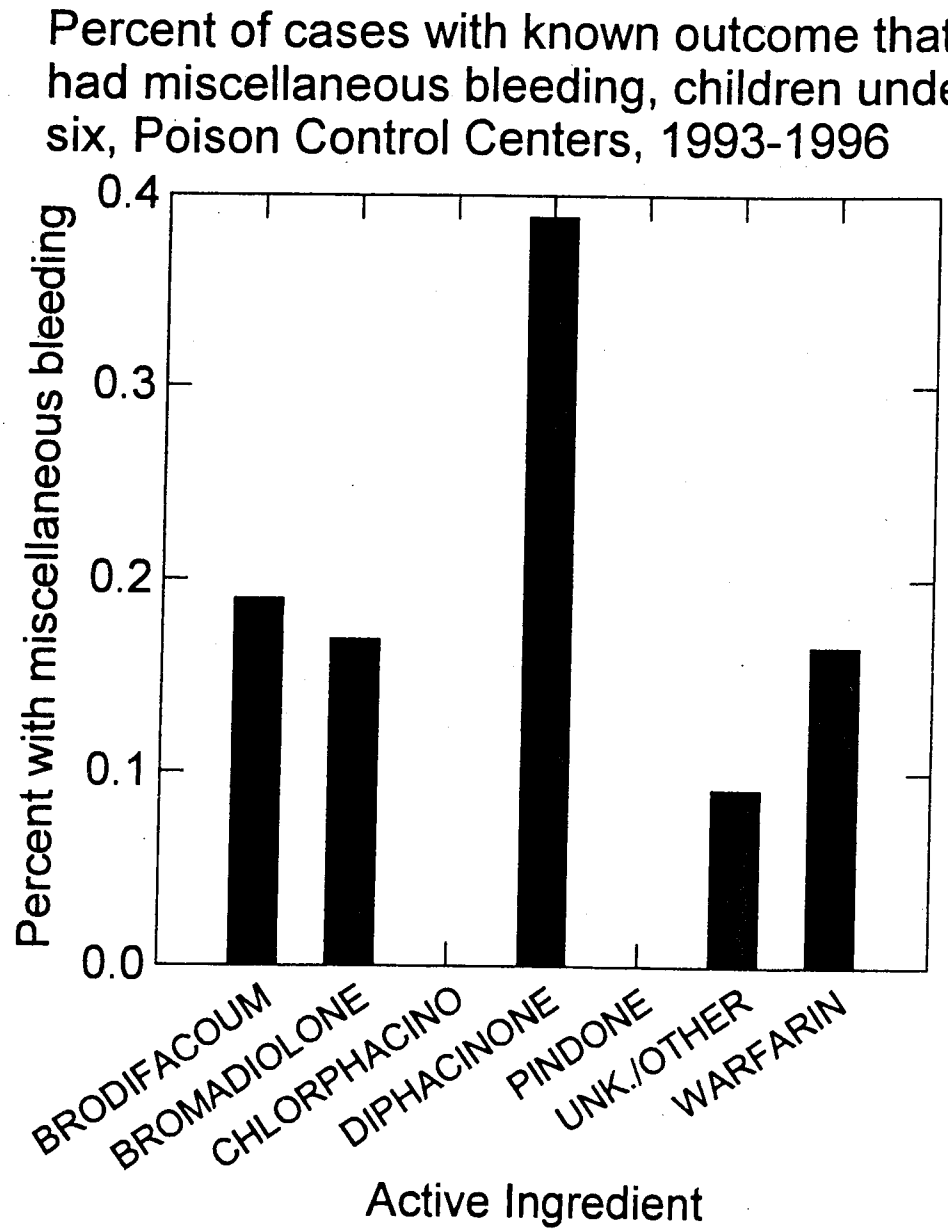

Figure 12. Percent of cases with known outcome that had bleeding among children under six years old reported to Poison Control Centers, 1993-1996, by active ingredient for anticoagulant rodenticides.

Summary

Anticoagulant rodenticides are responsible for a large number of exposures (over 12,000 per year, 1993-96) in children under six years of age, accounting for 20% of all pesticide exposures. Fortunately, the majority of these exposures, 97%, do not result in significant symptoms based on those cases which receive follow up to determine medical outcome. Compared to other major types of pesticides, anticoagulants were the least likely to have symptomatic outcomes, accounting for only 2.6% of the total symptomatic cases due to all pesticides. Despite the relatively low number of symptomatic cases, anticoagulants are much more likely to receive medical treatment accounting for 41% of all pesticide-related cases seen in a health care facility and 15% of all hospitalized cases.

Measures to prevent exposure and prevent unnecessary health care should be considered. Greater use of tamper-resistant bait stations and bittering agent are possible risk mitigation measures that could reduce exposure. A marking dye that would remain on a child's tongue after ingestion and improved education of health care providers might reduce the need for unnecessary medical care.

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Appendix 1. Instructions for converting AAPCC files

At DOS prompt:
1. Pkunzip a:\pest93fn.zip Then pest94fn.zip, pest95fn.zip, and pest96fn.zip
2. cd c:\dBASE
3. Database file select c: then pest93fn.dbf
go to dot prompt and type: append from pest94fn.dbf
.append from pest95fn.dbf
.append from pest96fn.dbf
.append form pest97fn.dbf
also from dot prompt:
4. DELETE for outcome="9"
5. COPY to c:\suicide.dbf for reason="09" .OR. reason="14"
6. COPY to c: multiple.dbf for generic_2 >1
7. DELETE for reason="09" .or. "11" .or. "12" .or. "14" .or. "18"
   DELETE for SUBST_NO > 2
   DELETE for Generic_2 > 1
8. PACK leaving single product, unintentional, outcome= 1 thru 8.
9. Modify structure in assist:

Add 62: ACTIVE charac 6		67: SYM numeric 1
63: AGECLASS charac 5		68: OUT numeric 1
64: HCF numeric 1		69: ICU numeric 1
65: TR_REL numeric 1		70: MOD2_4 numeric 1
66: HOSP_ADM numeric 1		71: LIFETH numeric 1

Also change MAN_SITE, REF_TOHCF, IN_HCF, OUTCOME, SUBST_NO, GENERIC_1, GENERIC_2, AGE, AGE_UNIT, UNK_AGE to numeric (rather than character) variables.

10. REPLACE AGECLASS WITH 'ADULT' FOR AGE>19 .AND. AGE_UNIT=1
REPLACE AGECLASS WITH 'ADULT' FOR UNK_AGE>3 .AND. UNK_AGE<12
REPLACE AGECLASS WITH 'ADULT' FOR UNK_AGE=13
REPLACE AGECLASS WITH 'CHILD' FOR AGE<6 .AND. AGE_UNIT=1
REPLACE AGECLASS WITH 'CHILD' FOR AGE_UNIT=2 .OR. AGE_UNIT=3
REPLACE AGECLASS WITH 'CHILD' FOR UNK_AGE=1
REPLACE AGECLASS with "CTEEN" for age>5 .and. Age<20 .and. Age_unit=1
REPLACE AGECLASS with "CTEEN" for unk_age=2 .or. Unk_age=3

12. REPLACE HCF WITH 1 FOR MAN_SITE=2
REPLACE HCF WITH 1 FOR REF_TOHCF>=1 .AND. REF_TOHCF<4
REPLACE TR_REL WITH 1 FOR IN_HCF=1 .OR. REF_TOHCF=1
REPLACE HOSP_ADM WITH 1 FOR IN_HCF>1 .AND. IN_HCF<4

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REPLACE HOSP_ADM WITH 1 FOR REF_TOHCF>1 .AND. REF_TOHCF<4
REPLACE ICU WITH 1 FOR IN_HCF=2 .OR. REF_TOHCF=2
REPLACE OUT WITH 1 FOR OUTCOME>=0 .AND. OUTCOME<5
REPLACE SYM WITH 1 FOR OUTCOME>=1 .AND. OUTCOME<5
REPLACE MOD2_4 WITH 1 FOR OUTCOME>=2 .AND. OUTCOME<5
REPLACE LIFETH WITH 1 FOR OUTCOME>=3 .AND. OUTCOME<5
```